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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/109,858	07/02/1998	MAHENDRA S RAO	T5530.CIP	4010

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EXAMINER	
HAYES, ROBERT CLINTON	

ART UNIT	PAPER NUMBER
1647	22

DATE MAILED: 12/05/2001

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.	Applicant(s)
09/109,858	Rao et al
Examiner	**Art Unit**
Robert C. Hayes, Ph.D.	1647

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on *Sep 20, 2001* .

2a) ☐ This action is **FINAL.** 2b) ☒ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *12, 15, 16, 21, 23, 24, 26-33, and 59* is/are pending in the application.

4a) Of the above, claim(s) _____ is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *12, 15, 16, 21, 23, 24, 26-33, and 59* is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

15) ☒ Notice of References Cited (PTO-892)
16) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
17) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____
18) ☐ Interview Summary (PTO-413) Paper No(s). _____
19) ☐ Notice of Informal Patent Application (PTO-152)
20) ☐ Other:

DETAILED ACTION

1. The Group and/or Art Unit location of your application in the PTO has changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Group Art Unit 1647.

2. The provisional rejection of claims 26 & 27 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claim 32 of copending Application No. 08/909435, is withdrawn due the submission of a terminal disclaimer.

3. The rejections of claims 12, 16, 23-24 & 26-33 under 35 U.S.C. 112, second paragraph, as being indefinite is withdrawn due to either Applicants' arguments or because of the amendment of the claims.

4. Applicant's arguments filed 9/20/01 have been fully considered but they are not deemed to be persuasive.

5. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

6. Claims 12, 15-16, 21, 23-24, 26-33 & 59 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of culturing cells from the rodent or human CNS using specific antibodies directed against specific epitopes to obtain a population of neuron-restricted precursor cells with the specific phenotype and morphological properties disclosed in the specification, does not reasonably provide enablement for broadly claimed cell culture methods where others are invited to define the required parameters to practice the claimed invention, or for claims directed toward using any antibody directed against unknown epitopes with no known structural characteristics. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims, for the reasons made of record in Paper No: 19, and as follows.

The specification describes on page 10 that "[p]referably, the selected antigen defining neuron-restricted precursor cells is embryonic neural cell adhesion molecule." However, no reference defining what constitutes such embryonic neural cell adhesion molecules, nor specific antibodies that specifically bind to any "embryonic neural cell adhesion molecule", are described within the specification. In contrast, the name, antibody to an "embryonic neural cell adhesion molecule", alone, sets forth no structural characteristics and little functional characterization for generating antibodies specific to a functional "embryonic neural cell adhesion molecule", and further encompasses any antibody directed to any biologically functional/active equivalent "embryonic neural cell adhesion molecule" as well as any randomly generated epitopes, which

are not described in the instant specification; nor known in the art. Moreover, the specification does not teach which particular amino acids are critical for detecting any embryonic neural cell adhesion molecule's function, nor what amino acid residues constitute a "embryonic neural cell adhesion molecule"- specific epitope; nor how to distinguish such from any different epitope specific for different proteins. Accordingly, random modifications, mutations, substitutions, additions, deletions or truncations of different "embryonic neural cell adhesion molecule"-related molecules/epitopes would be expected by the skilled artisan to result in antibodies that cross react with different proteins, or antibodies that no longer recognize the functional "embryonic neural cell adhesion molecule" required to practice the instant invention. For example, Geysen et al. teach that random amino acid changes to a tetrameric peptide/epitope, which includes conservative substitutions to the same antigen, have "frequently been associated with loss of antibody binding" (e.g., pg. 38, 1st col., 2nd *pp*). Thus, the lack of guidance provided in the specification as to what minimal structural requirements are necessary for any specific "embryonic neural cell adhesion molecule" antibody binding reaction would prevent the skilled artisan from determining what constitutes the desired antibodies required to practice the instant invention, because any random mutation or modification manifested within an embryonic neural cell adhesion molecule/epitope itself would be predicted to adversely alter its biologically active 3-dimensional conformation, and therefore, the antigenic site itself, without undue experimentation to determine otherwise.

Applicants argue on page 7 of the response that the "embryonic neural adhesion molecule antibody specific for the *sialylated form* of NCAM is commercially available ...." [emphasis added]. However, the claims are not directed toward this specific sialylated form of NCAM, nor have Applicants clarified the record that such is well known in the art, in order to successfully practice the instant invention as currently claimed. Therefore, although Applicants' arguments are persuasive, as it relates to no deposit is necessary, the current claims do not adequately structurally characterize the required E-CAM antibody required to practice the instant invention; thereby, requiring undue experimentation for the skilled artisan to known how to make and use the necessary components otherwise required to practice the currently claimed method.

7. Claims 21 & 59 stand rejected under 35 U.S.C. 112, second paragraph, as being indefinite and incomplete for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention, for the reasons made of record in Paper #19.

In particular, step (c) of claim 21 and step (b) of claim 59 merely state "via an embryonic neural cell adhesion molecule antibody", which recites no active method step itself (e.g., versus antibody capture, etc.); thereby, being ambiguous and constituting an incomplete method.

8. Claim 28 is rejected under 35 U.S.C. 102(e) as being anticipated by Boss et al. (U.S. Patent 5, 5,411,883).

Boss et al. teach a method of producing human postmitotic neurons by culturing cells that comprise neuron-restricted precursor cells in proliferating conditions (e.g., cols. 5-7, 9-12, Table 2-3), as evidenced by formation of aggregates/clusters/neurosphere clusters in a suspension culture of defined medium (i.e., in fresh F12 + 5% Chang's, and HN2 serum-free growth medium). Note that Boss et al. teach isolation of neuron-restricted precursor cells that express tyrosine hydroxylase, which reasonably express other common neuron markers, such as E-CAM. Methods of then using differentiating conditions to obtain postmitotic neurons are then disclosed by Boss et al. (e.g., col. 13-14).

It is noted that no "pure" population of neuron-restricted precursor cells are required in the instant method to distinguish Boss' method from claim 28.

9. Claims 21,23 & 26-27 are re-instated as being rejected under 35 U.S.C. 102(b) as being anticipated by Blass-Kampmann et al. (1994), for the reasons made of record in Paper 10, because, in contrast to that stated in the Office Action of Paper No. 19 (i.e., page 2), the current claims do not distinguish the instant claims from the method of Blass-Kampmann et al, because no antibody directed toward a *sialylated form* of NCAM is required in these claims.

10. Claims 12, 15-16, 24, 28-33 are re-instated as being rejected under 35 U.S.C. 103(a) as being unpatentable over Blass-Kampmann et al. (1994), in view of Boss et al, Weiss et al., Johe et al., Rao et al, and/or Lee et al., for the reasons made of record in Paper 10, because, in contrast

to that stated in the Office Action of Paper No. 19 (i.e., page 2), the current claims do not distinguish the instant claims from the method of Blass-Kampmann et al, in view of Boss et al, Weiss et al., Johe et al., Rao et al, and/or Lee et al., because no antibody directed toward a *sialylated form* of NCAM is required in these claims..

11. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL.** See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to examiner Robert Hayes whose telephone number is (703) 305-3132. The examiner can normally be reached on Monday through Thursday, and alternate Fridays from 8:30 AM to 5:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Kunz, can be reached on (703) 308-4623. The fax phone number for this Group is (703) 308-4242.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

RCH

Robert C. Hayes, Ph.D.
December 3, 2001

Gary L. Kunz
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SUPERVISORY PATENT EXAMINER
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